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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/302,241	09/08/94	WILSON R	CARPR0022C2

GUZO,D EXAMINER

18N2/1114

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ART UNIT	PAPER NUMBER
1805	25

DATE MAILED: 11/14/95

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined ☑ Responsive to communication filed on 7/26/95 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire three (3) month(s), _____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☑ Claims 51-61 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. ☐ Claims _____ have been cancelled.

3. ☐ Claims _____ are allowed.

4. ☑ Claims 51-61 are rejected.

5. ☐ Claims _____ are objected to.

6. ☐ Claims _____ are subject to restriction or election requirement.

7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8. ☐ Formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).

10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).

12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.

13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

EXAMINER'S ACTION

1. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

✓ 2. Claims 51-55 and 57-61 are rejected under 35 U.S.C. § 103 as being unpatentable over Sanders et al. in view of Alberts et al. or Watson et al., all further in view of Axel et al.

This rejection is maintained for reasons of record in the previous Office Action (Paper #20, Mailed 01/26/95) and for reasons outlined below.

Applicants have traversed this rejection, as previously applied, by asserting that Sanders et al. does not recite amplifiable vectors. In response, the examiner notes that

Sanders et al. has not been applied to teach amplifiable vectors. Applicants' indicate that since Sanders et al. teaches that the minimum amplification unit disclosed in Sanders et al. is 50,000 base pairs, the ordinary skilled artisan would have concluded that the GS gene would not have been suitable for use in a vector and would not have been motivated to look at the disclosure of Axel et al. Applicants also assert that none of the cited references teaches a vector encoding a complete glutamine synthetase gene as an amplifiable unit or an amplifiable vector. In response, it is noted that the Axel et al. patent, which is assumed to be enabled and accurate, was issued prior to the disclosure of Sanders et al. and discloses amplifiable vectors containing a mutant dhfr gene and heterologous DNAs, host cells transformed with said vectors, a method for introducing and amplifying nonselectable genes into host cells, use of the mutant dhfr gene as a dominant selectable marker, etc. (See Axel et al., Columns 26-30). It is unclear if the vectors disclosed by Axel et al. contained a complete dhfr gene, although Axel et al. refers to transfer of the amplifiable mutant dhfr gene and it can be assumed that a complete, amplifiable, dhfr gene was involved.

Applicants also assert that there is nothing in the cited references to suggest the advantage of the instant vectors with regard to their ability to amplify the GS gene and a foreign gene in cells containing an endogenous GS gene. In response, the examiner notes that this limitation is not recited in the claims. For example, Claim 51 recites a vector amplifiable in any host

cell, not specifically in a host cell containing an endogenous GS gene. Also, Axel et al. teaches cells transfected with a vector containing a dhfr gene, wherein said cells contain an endogenous dhfr gene.

Applicants also assert that since Axel et al. is directed to use of a mutant dhfr gene, the teachings of Axel et al. are not relevant to the instantly claimed subject matter, which recites a complete mammalian dhfr gene. In response, it is noted that applicants' claims recite a "complete" enzymatically active GS gene. A mutant dhfr gene as recited by Axel et al. is "complete" in that it is enzymatically active and only differs from a wild-type gene in that it is a dominant acting methotrexate resistant gene.

3. Claim 56 is rejected under 35 U.S.C. § 103 as being unpatentable over Ringold et al. (U.S. Patent #4,656,134, issued 4/7/87, see whole document, particularly Columns 5-7) in view of Sanders et al. and Watson et al. or Alberts et al.

Applicants recite a method of endowing a cell (possessing reduced or non-existent GS activity) with the ability to survive in a medium lacking glutamine comprising transforming said cell with an amplifiable vector encoding a complete mammalian GS gene.

Sanders et al., Watson et al. and Alberts et al. are applied as in the above 35 USC 103 rejection of Claims 51-55 and 57-61.

Ringold et al. recites a method for endowing a cell deficient in DHFR with DHFR activity (and hence the ability to survive in medium without glutamine) by transforming said cell

with an amplifiable vector containing the dhfr gene. While Ringold et al. do not definitively recite transformation with a vector containing the entire dhfr gene, Ringold et al. do recite transfection with a dhfr gene encoding an enzymatically active enzyme and given the teachings of Sanders et al. on the isolation of at least part of the CHO dhfr gene and the teachings of Watson et al. or Alberts et al. on cloning of genes of interest, it must be considered that isolation of the entire dhfr gene by the ordinary skilled artisan would have been an obvious, routine, matter. One would have been motivated to isolate the complete dhfr gene in order to be sure to express the entire biologically active gene product in cells lacking this gene so that cells could be properly selected for amplification of the selected genes. Given the routine nature of cloning procedures at the time the instant invention was made, it must be considered that the ordinary skilled artisan would have had a reasonable expectation of success in isolating the complete GS gene.

4. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention.

Applicants recite a method of endowing a "CHO-KI myeloma cell" deficient in GS activity with the ability to survive in media lacking glutamine; however, there is no written description of a "CHO-KI myeloma cell" in the specification, as filed. Also, applicants in the amendment filed 7/26/95, indicate that "...CHO-KI cells are not myeloma cells, but rather are derived from Chinese ovary tissue" (Page 13 of the amendment).

5. Claim 58 is rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

Applicants recite a method of endowing a myeloma cell (completely lacking or reduced in GS activity) with the ability to survive in a medium lacking glutamine, wherein said method comprises transforming said cell with an amplifiable vector containing a complete mammalian GS gene. However, applicants' specification provides no disclosure on what myeloma cells would be suitable for use in the instant method, how said cells are to be obtained, how said cells are to be cultured, how mutant cell populations lacking GS activity are to be generated, etc. If the

skilled artisan, finding no guidance or working examples in the instant specification would then look to the specification for citations of relevant prior art documents to provide guidance in reducing to practice the claimed method, said artisan would again be frustrated as applicants provide no citations of relevant prior art documents on how one of skill in the art would practice the claimed method on myeloma cells. Essentially, applicants are inviting the skilled artisan to practice trial and error experimentation to attempt to practice the claimed invention with myeloma cells. This type of experimentation is the antithesis of enablement under 35 USC 112, 1st paragraph and said experimentation must be considered to be undue and excessive.

6. Claims 57 and 59 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

7. Claims 51 and 55 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 51 (and dependent Claim 55) are vague in that applicants recite a DNA expression vector "...which is capable..." of expressing a GS encoding gene. The capacity of a product to accomplish some function is vague in that the claim language is not definitive and implies some other, undisclosed, capacities and is not proper claim language. Redrafting the

claim to read on "A recombinant DNA expression vector which is amplifiable in a transformed host cell and which expresses, in said transformed host cell, a recombinant DNA..." would be remedial.

Any rejections not repeated in this Action are withdrawn.

No claims are allowed.

Certain papers related to this application may be submitted to Art Unit 1805 by facsimile transmission. Papers should be faxed to Art Unit 1805 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (Nov. 16, 1993) and 1157 OG 94 (Dec. 28, 1993) (See 37 CFR 1.6(d)). The Art Unit 1805 fax number is (703) 308-4312. NOTE: If applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo whose telephone number is (703) 308-1906. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mindy Fleisher, can be reached on (703) 308-0407. The fax phone number for this Group is (703) 308-4312.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

DAVID GUZO
PATENT EXAMINER
GROUP 1800

David Guzo
November 2, 1995